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RADIUM

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AND
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VOL. IX JULY, 1917 No. 4

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. IX JULY, 1917 No. 4

RADIOTHERAPY IN GYNECOLOGY*

F. E. KEENE, M. D., PHILADELPHIA.

This report comprises an analysis of 116 cases treated in the Gynecological Department of the University Hospital. Of this number sixty-nine were malignant growths of the cervix, vagina and urethra, and forty-seven were cases of benign hemorrhage of myomatous or myopathic origin. [1]

MALIGNANT CASES.

We have been unable to obtain the present condition of ten patients, leaving fifty-nine for our analysis. Treatment was undertaken in all cases irrespective of the extent of the disease and, with but one exception, all had passed the operable stage. I wish to emphasize the fact that radium was applied to these inoperable cases, not with the idea of cure but to relieve excessive hemorrhage and discharge. In the majority, the diagnosis was confirmed by microscopic examination; the remainder presented such characteristic gross appearances as to offer no question of doubt concerning the nature of the lesion.

Profuse, irregular hemorrhage was the chief symptom in forty-five cases. In forty-two, the application of radium was followed by complete cessation of bleeding. Of this number, thirty-four have had no return and in eight reappearance of bleeding is noted in from three weeks to eight months after the treatment. In but three cases was hemorrhage uninfluenced. Foul, irritating discharge was an additional complaint in thirty-five patients. Twenty-two of these were entirely relieved within a few weeks, while in thirteen there was either a decided decrease or no effect whatever.

*Penna. State Med. Journ. Vol. XX., pp. 469-472, April, 1917. Read before the Section on Surgery of the Medical Society of the State of Pennsylvania, Scranton Session, September 20, 1916.

1. I am indebted to Drs. John G. Clark, Brooke M. Anspach and C. C. Norris for the privilege of including their cases in making this report.

The statement has been made that radium not infrequently relieves pain, but this has not been confirmed by our experience. Nineteen patients suffered pain of varying severity and in but two of these was this completely relieved. In the remaining seventeen, the pain continued as before the application, or increased as the malignant process extended.

Five cases of rectovaginal or vesicovaginal fistulae developed subsequently. In four months elapsed between the treatment and the development of the fistulae, therefore it seems likely that these are to be ascribed to an extensive sloughing of the growth and not to the direct action of radium. In the fifth case of fistula, radium was applied in the vaginal cuff immediately after a total hysterectomy, and here fistulae involving both bladder and rectum appeared in four weeks, due doubtless to the effect of radium on tissues whose resistance was lessened by the trauma incident to operation.

Technic of Application.—The majority of cases received from 85 to 110 milligrams for twenty-four hours; 210 milligrams were applied in one case of a large cauliflower growth in a woman of 28 who was six months pregnant. The radium was encased in a platinum capsule and rubber dam covering. When ulceration was present, the curet was used only to obtain sufficient tissue for microscopic examination. In the cauliflower type, the friable mass was removed with the fingers or lightly curetted and cauterized or packed to control hemorrhage, and radium was then applied, thus promoting deeper penetration. As a rule, these patients remained in the hospital one to three days after the application. The patients were advised to return in five weeks for examination and a second treatment.

Results.—The only immediate constitutional effects which followed the application of radium were nausea and vomiting, which usually ceased in from twenty-four to thirty-six hours after the radium was removed. Rarely, there was an elevation of temperature which reached 100 to 103 F., but this was of short duration. In a few instances the patients complained of vesical and rectal irritability. The local effects of radium are very striking and are to be seen in every favorable case within a few weeks after the application. The ulceration rapidly becomes healthy in appearance and diminishes in size or entirely disappears, leaving a dense, white, smooth scar surrounded by an intensely red vaginal mucosa. Later, as the scar tissue contracts, there is narrowing of the vagina and light adhesions may unite the anterior and posterior vaginal walls. During the process of healing, a profuse, purulent discharge is not infrequently noted, but this disappears in the course of a few weeks.

Remote Results.—In twenty-six, or 44 per cent. of our cases, there has been complete healing of the carcinomatous ulceration in the cervix or vagina, leaving merely a white scar at the site of the growth. Two of these show no evidence of carcinoma twenty-two months after the first application of radium. Two cases of chorio-epithelioma of the vagina are well with no local evidence of disease after sixteen and twenty-one months, respectively. In the case of carcinoma complicating pregnancy, a portion of the mass was removed with the cautery and radium applied immediately. Six weeks later the patient gave birth to a normal child with no complications, and at the present time, four months after the first treatment, she enjoys perfect health with no evidence of carcinoma remaining. The time in the other cases varies from two to twenty-one months and in several of these, while there is local healing,

the deeper extension of the process continues, showing that radium has little if any effect beyond certain limits. The ulceration in six cases has been greatly lessened, while in twelve there is no local effect apparent or the spread of the disease has been hastened by the treatment. We have been unable to ascertain the local results in eleven cases. Thirteen patients have died at intervals varying from one to eleven months after the radium was applied.

Benign Cases

This series of forty-seven cases comprises patients who have been treated for uterine hemorrhage of myomatous or myopathic origin. In no case was the tumour of large size and, in each, the only symptom was excessive bleeding.

Technic of Application.—In every case a preliminary curettage was performed and the curettings examined to eliminate carcinoma of the fundus. The radium, protected by platinum and rubber, was inserted to the fundus of the uterus, where it remained for from eight to thirty hours. In by far the larger number of cases the time of application was twenty-four hours, and the amount of radium 50 milligrams. The patients were discharged from the hospital in from three to five days after operation.

Results—As in the cancer cases, nausea and vomiting not infrequently followed, lasting one or two days. Occasionally there was slight elevation of temperature, and in one instance 103 F. was reached. As a rule, the convalescence was marked by no disagreeable symptoms.

We have obtained the results in all but two cases, and in not a single instance has there been a failure to check the bleeding. Four patients were between 20 and 30 years of age, in whom the application was made for only eight hours; in these, the profuse menorrhagia has been reduced to the normal flow. In the remaining forty-one, the periods have entirely ceased for intervals varying from two to nineteen months. Amenorrhea may immediately follow the application of radium, there may be one or at most two scanty periods, or slight, irregular bleeding may occur for a few weeks before the permanent amenorrhea is established. In three cases a scanty flow was seen after several months but this was again followed by amenorrhea.

We have been interested in the action of radium as regards its effects on leukorrhea. Our results show that, in the majority of cases, no discharge follows its application. Rarely, a profuse discharge may be present for a few weeks, but is not permanent. Ten of our patients gave the history of profuse leukorrhea and this has been entirely relieved by the radium. In this we have been agreebly surprised, since it seemed logical to assume that the changes produced in the endometrium and uterine blood vessels might lead to a permanent and troublesome discharge.

Abdominal or pelvic pain has followed in three cases, coming on immediately after the application and lasting for ten days. It is of interest to note that mild symptoms of the menopause have been developed in ten cases.

The only ill result occurred in a case of chronic pelvic inflammatory diseases in which the patient's chief complaint was excessive and irregular menstruation. Here there was evidently a lighting up of the old process, since two days after the application the symptoms of acute pelvic peritonitis developed and at operation a few weeks later the findings were those of an old infection with a superadded acute process.

Conclusions.—Based on the foregoing analysis as well as a review of our operative statistics in both malignant and benign conditions of the uterus, we have formulated the following conclusions which govern us in our work.

Because of the large percentage of permanent cures in even fairly advanced cases of carcinoma of the fundus, operation is the treatment of choice and radium should not be used. In carcinoma of the cervix, there is not sufficient data at hand to determine the permanent cures produced by radium after the five-year interval. Therefore, in all cases of early cervical cancer, radical operation is to be advised. In the more advanced stages, which are questionably operable, the application of radium is the procedure of choice. In such cases, if radium has produced an apparent cure, operation at a later date with the idea of further eradication of the disease is inadvisable. The application of radium in the vaginal cuff immediately after radical operation may be followed by disastrous sequelae.

For the control of hemorrhage and foul discharge in cases beyond the operable stage, radium is by far the best means at our disposal and under such circumstances it should be looked on as a palliative and not a curative measure. Even these cases may exhibit what is apparently a complete cure but as yet sufficient time has not elapsed to warrant any definite conclusions. In a certain percentage of cases radium will have no effect on the growth or may stimulate it to more rapid extension. The majority, however, show a rapid destruction of the cancer area with local healing of the ulceration in over 40 per cent. In many of these cases of local eradication of the superficial growth, the deeper extensions or metastases are little if at all affected; hemorrhage and discharge will be controlled but the advance of the disease will be unchecked.

Benign Hemorrhage.—Radium is the treatment of choice in all cases of small, uncomplicated myomata, whose only symptom is hemorrhage. In these as well as in cases of myopathic hemorrhage, 100 per cent. cure can be expected. Sufficient dosage will produce complete and permanent amenorrhea. In young women, radium should be used with the greatest caution, since its application may be followed by a premature menopause. If other measures have failed, radium may be employed, but in small dosage. Irregular bleeding due to pelvic inflammatory disease, tumors of large size or tumors of any size complicated by disease of the adnexa or surrounding structures, as well as myomata in young women, are to be treated by appropriate operation and not by the application of radium. In no case of uterine bleeding should radium be used without a preliminary curettage and microscopic examination of the curettings by a competent pathologist. In properly selected cases the immediate convalescence is smooth and restoration to health is complete. Pelvic pain rarely occurs and as a rule is of but a few days' duration. In the exceptional case profuse leukorrhea follows the application of radium, but this is not permanent. Not infrequently radium has cured or diminished discharge which was present before its application.

In this brief summary I have attempted to give a fair and unbiased statement of the benefits, limitations and dangers of radiotherapy in gynecology. Our conclusions of today may be completely changed by our experience of tomorrow for the entire field of work is still in the period of probation.

DISCUSSION.

DR. HENRY K. PANCOAST, Philadelphia: I occupy the rather peculiar position of one who praises the work of another man who takes work away from him. Most of the cases Dr. Keene has cited are such as have been or may be benefited by Roentgen rays. I have closely followed the work done by Drs. Keene, Clark and Anspach at the University Hospital, having been engaged in the general use of radium in that institution, with the exception of the gynecological work, which has been entirely under the care of the gynecological service. I have kept in touch with their work and can endorse all that Dr. Keene has said. The gynecologist has the advantage over the roentgenologist in that he is able to use this agent himself; whereas the roentgenologist is usually not a gynecologist. There are undoubtedly some advantages in radium over Roentgen rays in this one feature.

I will discuss particularly the treatment of carcinoma of the cervix. It would be well to state for the benefit of those who ever refer patients for radium treatment that there are certain carcinoma cases in which nothing can be expected by radium or Roentgen therapy, or any other method that is now known or may be discovered in the future. They are cases in which the removal of the growth itself would endanger life or cause death by exposing important organs or structures. Such a case was referred to me a few days ago, and the patient was in turn sent to Dr. Keene for his opinion. Roentgen or radium therapy could have accomplished nothing because it would have meant opening up the bladder and the rectum, and the patient would have been in worse condition than if left alone. The results of radium therapy in carcinoma of the cervix cannot be classified as cures as yet, because the longest cases have still almost three years to run before they come within the five-year period. There must be certain cases in which it is just possible for a recurrence to take place along the borderline, because the application of radium is not quite sufficient to control the disease. We must remember that the penetration of radium rays with destructive effects is limited. There is a certain point at which destruction ceases and, in fact, growth may be stimulated. Roentgenologists contend that these are cases in which a combination of treatment might do good by the Roentgen rays supplanting the radium rays where the destructive effect of the latter weakens at the outer border of the growth in the broad ligament or wherever it may be.

RADIUM TREATMENT AT THE ROYAL INFIRMARY, EDINBURGH.*

The following abstract of the report to the managers on radium treatment at the Royal Infirmary, Edinburgh, during the year 1916 has been sent to us for publication by Dr. Dawson Turner, who is in charge of the radium treatment at the infirmary.

Sixty-six patients attended for radium treatment during the past year, whereas 64 attended during the previous year. The total attendances during the year were 520. Of the 66 patients half were inpatients from other departments of the infirmary. Twenty-eight suffered from rodent ulcers, 25 from inoperable malignant disease, 7 of these affecting the vagina or cervix uteri. There were 7 cases of ex-

*Reprinted from The Lancet, Vol. CXCII., April 7, 1917, pp. 546-7.

ophthalmic goitre and 4 of naevi. Amongst the malignant cases there were 8 sarcomas and 17 carcinomas. The former are more amenable to radium than the latter, and sometimes disappear in a remarkably short time. They are, in the writer's experience, invariably benefitted by radium treatment, and if accessible and localized can be entirely removed. Rapidity of growth is no contraindication to the use of radium, for rapidly proliferating cells are very vulnerable to its radiation; there is, in fact, reason for believing that they are more vulnerable than cells which in morphology and growth more nearly resemble the normal. This has been brought to the writer's notice on certain occasions. This leads to the important question, "Are all sarcomas equally amenable to radium treatment?" If a negative answer must be given to this—then what conditions determine a tumor's sensitiveness? Gaarenstroom, of the Amsterdam Cancer Institute, [1] is of the opinion that the histological structure is the chief criterion and that round-celled sarcomas generally react favourably, spindle-celled less so, and polymorphous-celled least so. He bases this opinion upon an experience of 23 cases treated by the Roentgen rays. He made no use of radium and the effect of radium rays may not be quite the same as the effect of Roentgen rays. At any rate, the writer has frequently had rodent ulcers sent to him for radium treatment which have been treated unavailingly by Roentgen rays, and these rodents radium has cured. This may have been due, it must be admitted, to a more appropriate dosage and closer apposition. Myelosarcomas, lymphosarcomas, large spindle-celled sarcomas, and parotid mixed-celled tumours are extremely sensitive, in the writer's experience, to radium rays. (*Vide* Cases 1, 3, and 10.)

Malignant disease of the vagina and cervix is favourably affected by radium treatment, and epitheliomas, if localized, can confidently be expected to disappear. Owing, however, to the difficulty of efficiently raying the more inaccessible portion of the growth, recurrence in these positions after a longer or shorter period of time is common. This can be again subjected to treatment, but, as a rule, less successfully than the primary growth, and this for two reasons; the one that the recurrence is probably situated in a less accessible position, as in an extension to the broad ligaments; the other that after a course of raying only those cells survive which are refractory to the rays and a recurrence consisting of such cells or daughter cells is less susceptible to attack. There is a tendency by natural selection to breed cells which are immune. The same phenomenon can sometimes, though rarely, be observed in rodent ulcers; an extended ulcer attacking perhaps bone or mucous membrane after repeated raying does not respond at all. In these cervical cases, even though there should be recurrence, the patient has greatly benefited in the meantime by the removal of pain, the cessation of discharges, and the general gain in health and strength. This gain in general health may be striking and equivalent, as some of the continental authorities have termed it, to a virtual resurrection. (Cases 6, 7, and 8.)

As observed in last year's report, rodent ulcers require no detailed notice, for the beneficial action of radium is generally admitted. Uncomplicated cases situated on the skin and not too extensive for the amount of available radium invariably do well. If they recur, which may be due to an insufficient primary treatment, they easily yield to a second course and remain cured. The cosmetic result leaves nothing to be desired, and there is scarcely any subsequent contraction of the skin.

1. Archives of Radiology, December, 1916.

They are less amendable when situated on mucous membrane. Though a single strong application may suffice to remove the rodent, the writer prefers, when it is possible, to divide the necessary dose into two or three administered at three or four days' interval. It is important, in order to prevent a recurrence, that the deeper parts as well as the superficial should receive adequate treatment.

Seven cases of exophthalmic goitre, five females and two males, received radium treatment. All benefited save one, an acute case, who died, in less than a month after the treatment, of hyperthyroidism. As mentioned in last year's report, indisputable benefit is occasioned without any necessary obvious change in the organ, though generally it is diminished in size. I would again draw attention to Rave's experiments [2] on cats and rabbits. He administered large doses of X rays to the thyroids of these animals, and found from subsequent histological examination that no recognizable changes had been produced. Confirmatory results have been obtained by others. It appears, then, that in the thyroid gland we have a structure which, so far as histological examination can carry us, is refractory to X rays. Yet there is ample clinical evidence of the beneficial effects of irradiation in exophthalmic goitre.

The following are brief notes of the more important cases treated except rodent ulcers, which have been purposely excluded. Reference has also been made to one or two old cases whose progress it has been possible to follow.

CASE 1.—Myelosarcoma of temporal region involving orbital cavity in a male aged 23, recommended by Professor Gulland. Admitted October 17th, 1916. Duration three years. Began by headaches and swelling of jaw. A small operation was performed to remove the swelling. Later a tumour appeared on the right temporal region. On July 7th, 1916, Professor Caird excised a fragment which was found by the pathologist to be a myelosarcoma. Professor Caird refused to operate. On admission there was a prominent swelling over the right temporal region accompanied by shooting pain, difficulty in opening the mouth, and strabismus. An X ray showed that the frontal bone and upper jaw were involved. On November 1st, two radium tubes were inserted in Mr. Dowden's absence by Dr. White into the growth, and external radium treatment was also begun. A total dose of 4920 mgh. was administered. In a week's time the growth had diminished in size, the headache was better, and the jaw was freer. On November 28th, 1916, there was no squint and no pain. Professor Gulland examined him and wrote: "I was delighted to see the patient today and to find that he had improved so very greatly. He looks immensely better, and I see no reason why he should not start work." On January 23rd, 1917, he continued quite well.

CASE 2.—Scirrhus in a female aged 59, recommended by Dr. David Huskie. Admitted November 28th, 1916. A year ago Professor Caird removed patient's left breast for scirrhus. In the line of the scar there is an ulceration with hard borders. It has been burned by Dr. Huskie three times. This ulcer was given a dose of 205 mgh. during a fortnight. A week later Mr. Jardine examined her and wrote: "Result very successful, no more need for treatment." The ulcer and hardness had disappeared. Warned patient to report herself regularly to Dr. Huskie.

CASE 3.—Recurrent sarcoma (old case) in a female aged 49, recom-

2. Vide Colwell and Russ, Radium and the X-rays, p. 212.

mended by Dr. Maclagan. Duration four years. Several operations for the removal of the growth without success. Admitted by Mr. Miles on July 15th, 1915. Now a large nodular mass projecting in the left suborbital region and adherent to the maxilla. Pathological report, large spindle-celled sarcoma. As Mr. Miles considered the tumour inoperable radium treatment was commenced. By internal and external applications a dose of 5880 mgh. was given. In November, 1915, she was readmitted. There was now an ulcerating mass closing the left eye, the mass was so friable that it was difficult to keep tubes embedded, but by external treatment a dose of 5180 mgh. was given. During these applications the growth diminished markedly. On February 1st, 1916, the tumour had greatly shrunk and was moveable; it had been fixed before. Patient better and stronger and can see normally. The condition had so much improved that Mr. Miles removed what was left of the growth, and further radium treatment was commenced. A dose of 4120 mgh. was given as a prophylactic against recurrence. On November 23rd, 1916, the growth had disappeared, an area of dead bone was visible, the skin around healthy. Mr. Miles could detect no sign of recurrence.

CASE 4.—Sarcoma involving lower ribs on right side in a male aged 44, recommended by Mr. Dowden. Admitted May 15, 1916. Duration about 18 months. On account of a swelling in the region indicated the patient attended the surgical out-patient department of the Royal Infirmary in October, 1915, and Mr. Jardine scraped the interior of the growth. The pathologist reported that the growth was a sarcoma. The growth never went quite away, and on April 25th, 1916, the patient was admitted to Mr. Dowden's wards. The tumour was now increasing, and as Mr. Dowden was of opinion that an operation would be an extremely severe one he thought that radium might be tried. Over the growth there was a cyst containing blood. Radium treatment was now begun. Three tubes of radium were inserted into the substance of the growth and a total dose of 7560 mhg. was administered. On June 14 there was considerable external swelling and discharge. On July 20th the external swelling was less, but there was more pain. The patient reported himself at regular intervals and appeared to be gaining strength, for on November 21st, 1916 he asked permission to resume his work as a brass finisher. This Mr. Dowden permitted him to do. On January 2nd, 1917, he was well and hard at work but above the original growth there was a hard tumour mass, which Mr. Dowden had noticed before.

CASE 5—Myeloma in a female aged 23, recommended by Mr. Dowden. History: Two years ago patient complained of a gumboil on the right side of the superior maxilla. Dr. Gibbs found a growth and recommended her to consult Mr. Dowden. The latter scraped out the cavity and the pathologist reported the growth to be a myeloma. It lay posterior to the superior maxillary bone. As a prophylactic radium treatment was recommended, a tube of radium was attached to a wire and passed up into the cavity, and a dose of 1920 mgh. administered. This was in October, 1915. In February, 1916, there was no trace of a recurrence, but when the patient reported herself in June, 1916, Mr. Dowden found that the disease had returned. On June 27th Mr. Dowden scraped out the cavity and inserted radium tubes, at first three, but on one coming out only two were kept in. A dose of 4400 mgh. was now given, more than double the dose she was given the first time. Precautions were also taken to attempt to maintain the radium in a more effective

position. Very severe reaction followed with swelling and pain, which required constant opiates, the tongue and mucous membrane of the cheek being burned. In December the patient was much better, and on January 2nd, 1917, Mr. Dowden could find no trace of a recurrence.

CASE 6.—Sarcoma of cervix in a patient aged 47, recommended by Dr. Barbour. Admitted July 20th, 1916. Duration one year. Complains of a bearing-down pain and some discharge. On June 26th, 1916, the cervix, found to be ulcerated by Dr. Fordyce, was curetted. Pathological report, sarcoma. Dr. Barbour examined her on July 20th, 1916, and found hard nodules all around the cervix except posteriorly. The right ligament was thickened. Body of uterus unaffected. Hysterectomy unsuitable. A dose of 4300 mgh. of radium was given. September 26th, 1916: Examined by Dr. Fordyce. Condition very satisfactory, there being no trace now of the indurated nodules, but cicatrisation instead. November 14th, 1916: Parts seemed quite healthy; no discharge; patient much stronger. Weight 8st. 1½ lb. February 1st, 1917: The patient was examined and the parts found to be *in statu quo*.

CASE 7.—Squamous epithelioma growing from vaginal roof behind and to left of cervix in a patient aged 63, recommended by Dr. Orr and Dr. W. Fordyce. Admitted October 16th, 1916. There is a soft fungating gangrenous mass of the size of a Victoria plum occupying the above position. This was removed by operation and the base of it thoroughly scraped and pure carbolic acid applied. Pathologist report: Squamous epithelioma showing marked necrosis. Ten days later the mass had grown again to half its previous size; very foetid discharge; some necrosis. The mass was again removed and radium applied to base and a dose of 4900 mgh. administered. January 11th, 1917: Dr. Orr writes, "There is today nothing to be felt except a cicatrix and the least suspicion of ulceration, perhaps the size of a green pea, at one point of the cicatrix. The patient feels and looks well and the result so far is very gratifying."

CASE 8.—Epithelioma of the cervix. (An old case.) Patient, aged 30, recommended by Dr. Brewis. Admitted July 6th, 1915. Complaint of loss of health and reddish-brown discharge. Cervix widely involved; uterus fixed. After curetting a dose of 6720 mgh. of radium, September 30th: Patient much better. Pain disappeared. Cervical cavity smaller, granulations superficial, a scraping still showed squamous epithelioma cells. Uterus movable. In consequence of pathological report a dose of 1920 mgh. was given. February 3rd, 1916: Patient greatly improved, looks another woman. July 20th, 1916: Quite well. Uterus shrivelled, replaced by granulation tissue. Pathologist's report from a scraping. November 16, 1916: Returned to ward complaining of continuous pain in right leg. Examined by Dr. Brewis under chloroform. Cannot feel cervix or body of uterus, but to the right there was a hard mass in the position of the broad ligament extending back to the sciatic notch of the bone. The mass is a good size and fixed. A scraping showed malignant cells. A dose of 6,500 mgh. of radium was administered. December 14th, 1916: Rise of temperature. Examination showed that the opening to the cavity was blocked. A drainage-tube was introduced. January 15th, 1917: A slough came away. Temperature still rises but less, pain also less and only felt at night. Patient remains in a prostrate condition, due to the disease and to the destruction produced by the radium. February 2nd, 1917: Patient remains *in statu quo*.

Case 9.—Chondro fibro-sarcoma in a boy, aged 6, recommended by Dr. J. S. Fraser. Admitted May 9th, 1916. The disease affected the left maxillary antrum, causing protrusion of the cheek, diplopia, and proptosis. Dr. Fraser removed as much as was possible of the growth by scraping, but fearing that he had not eradicated it consulted with Mr. Dowden with a view to the removal of the left superior maxilla. Mr. Dowden, however, was of the opinion that the case was more suitable for radium. Tubes of radium were introduced through an opening into the mouth and a dose of 1440 mgh. administered. The patient was examined on January 3rd, 1917, by Dr. Garretson, in the absence of Dr. Fraser, and he was unable to detect any sign of the disease. The boy appears to be perfectly well and is attending school.

Case 10.—Myeloma of the sternum (old case) in a male aged 23, recommended by Professor Gulland. Admitted March 9th, 1915. Duration two years. Growth the size of a large cocoanut adherent to sternum. Symptoms: weakness and dyspnoea. Consultation with Mr. Miles, who considered the case inoperable. Four radium tubes were introduced by Mr. Miles into the growth and radium was also applied externally. A dose of 13,200 mgh. was administered. Within a month of this treatment the growth had entirely disappeared. Professor Gulland remarked, in regard to this case, "that he had watched the tumour growing during the past 18 months, that it was of very large size, quite as big as two fists, that he had been rather a sceptic as regards the value of radium in malignant disease, but that he was now quite converted. The growth was a myeloidsarcoma." The patient recovered his health and strength and went back to work. Six months' later a small recurrence appeared over the sternum. After a dose of 250 mgh. it disappeared, but was followed by an ulcer about 1 inch deep extending into the eroded sternum. No pain was associated with the ulcer, which slowly filled up. The patient had a course of iodide of potassium on Mr. Mile's advice. The patient was able to continue with his work. On January 13th, 1916, patient was able to continue with his work. On January 13th, 1916, Professor Gulland wrote: "This patient had a long course of inunction and of iodide of potassium before the radium treatment, but without the slightest effect. The ulcer has impressed me more as a continued destruction of the tumour, which must have started from the centre of the sternum." The foregoing appeared in last year's annual report. The further history is as follows. In February, 1916, a swelling occurred in the left axilla, which was removed by Mr. Miles in March 1916. The pathologist's report was the following: "A difficult growth to classify. There is a large amount of well-developed fibrous tissue. The cells have a tendency to arrange themselves in rounded follicles. They are polygonal in shape and suggest endothelial cells in appearance and arrangement. The condition I regard as a tumour formation belonging to the group of the lymphosarcomata but somewhat anomalous in character." October 26th, 1916: The ulcer on the sternum is quite healed and the patient perfectly well.

THE AMERICAN RADIUM SOCIETY.

The second annual meeting of the American Radium Society was held in New York on June 4th, 1917, at the Vanderbilt Hotel. Following the President's address, on The Established Value of Radium as a

Therapeutic Agent, by W. H. B. Aikins, M. D., of Toronto, the following papers were read:

Radium in Dermatology, by Frank E. Simpson, M. D. (Chicago.) Radium in Gynecology, by John G. Clark, M. D. (Philadelphia.) Radium as an Aid in General Surgical Practice, by John M. Lee, M. D. (Rochester, N. Y.). Distance as a Factor in the Local Application of Radium, Charles H. Viol, Ph. D. (Pittsburgh.) In the absence abroad of Dr. Hugh H. Young, who was to have read a paper on New Instruments and Methods for the Application of Radium to the Rectum, Urethra and Bladder, Winfield Ayres, M. D., of New York, discussed the Technique of the Application of Radium to the Rectum, Urethra and Bladder. Histological Findings in Radiumized Tissue, Henry Schmitz, M. D. (Chicago.)

The meeting was well attended, and in the evening the members enjoyed an informal dinner.

REVIEWS AND ABSTRACTS.

John Joseph Nutt, M. D. (New York.) A Preliminary Report on the Use of Radium in Mobilizing Joints Having Fibrous Ankylosis Following Tuberculous Arthritis. The American Journal of Orthopedic Surgery, Vol. XV., No. 2, pp. 137-141, February, 1917.

The excellent results reported in the use of radium in mobilizing joints stiff from attacks of arthritis deformans, led me to consider radium as of possible use in mobilizing joints stiff as a result of tuberculous infection. It is not at all infrequent to have a joint left immobile after the cure of a tuberculous arthritis, even when no bony ankylosis exists. It is always a temptation to use force under an anesthetic to recover this lost function. So great is the benefit of a movable joint, that each surgeon must learn from experience before he can appreciate the grave risk involved in such an operation.

My experience with radium leads me to hope that in it we have a safe method of mobilization. The softening with radium of dense fibrous tissue might be expected to be as dangerous as is its rupturing by manipulation, but the slower action of radium gives nature an opportunity to remonstrate before irreparable damage is done, and, furthermore, nature can build new protective material as the old is destroyed.

Whether or not radium increases the bactericidal properties of the blood, whether it raises the opsonic index, has not been determined, but I felt that it would not lower the body's resistance to infection, and that experimental work was justifiable. Very small doses have been used, and we have felt our way carefully over this new ground.

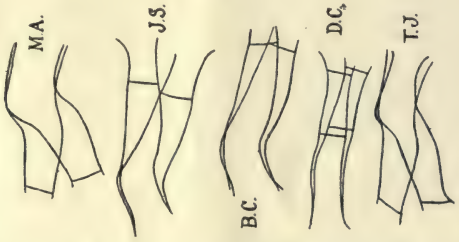
These cases I report had been sufficiently long without any sort of protection to justify a diagnosis of cured tuberculous arthritis with fibrous ankylosis.

In one case an anesthetic had been given and the joint forcibly manipulated. The result had been swelling, pain, local temperature, and a return of spasm, so that immobilization was necessary for several weeks. This knee had entirely recovered from this condition five months before radium treatment was instituted, the knee having been benefited not at all by the operation.

Another one of these cases had received attempts at passive motion

daily for a period of eight weeks, also the application of superheated air for about the same period, without any improvement.

All of these cases were tuberculous arthritis of the knee. They were all tested for von Pirquet reaction, which was positive in every case. The Wassermann test was negative.



Outlines of knees in positions of greatest extension and greatest flexion. Absolutely no movement was present when treatment was begun. Letters refer to cases reported.

Case 1. M. A. Admitted to the hospital, April 27, 1911, age 10 years. Unable to walk without crutches; knee deformed, with flexion at 45°; disease very acute. The latter part of 1914, all acute symptoms had subsided, leaving the knee posteriorly dislocated to a slight degree, with fibrous ankylosis. No protection to the knee was necessary. Persistent attempts had been made during a period of six months to mobilize the knee, without effect. Passive motion, massage, hyperemia by passive congestion, and hot air were all tried. Radium treatment was begun in January, 1915. A radium pad containing 50 micrograms of radium element, was applied to her knee at night, and finally was left on day and night. March 30, the movement in the knee was very perceptible. At this time radium solution was given three times a day, each 2 ounces containing 2 micrograms. This was continued for a month. Movement continued to increase slowly. In July, the use of the pad was discontinued. In September, patient mentioned a slight stiffness in the knee after sitting; the pad was reapplied and the stiffness disappeared within a few weeks. In February, 25 micrograms of radium element were injected intravenously. The outlines of the knee in extension and flexion, taken frequently, showed a steady progress in the movement. The diagram shown was taken on May 1, 1916.

Case 2. J. S. Admitted to the hospital in 1909. Pain severe, knee fixed in position of 40° flexion, with swelling, heat and muscular spasm. This case yielded very slowly to treatment. All acute symptoms disappeared the latter part of 1912. He was allowed to go without any protection for three months, when it became necessary to reapply a brace. This condition again cleared up, and he was considered cured six months later. There was no movement in the joint, and passive movement, without an anesthetic, was attempted. No improvement. A radium pad was applied in January, 1915, and this treatment kept up for several months. During this time the patient himself thought the knee much improved, but the increase of motion was very slight. Radium emanation water was then given, containing 17,000

mache units per liter. He was given of this two ounces three times a day. He received the following injections intravenously:

1915 Feb. 17	10	micrograms,	radium	element
Feb. 26	10	"	"	"
Mar. 9	10	"	"	"
June 24	25	"	"	"
July 23	25	"	"	"
Nov. 5	50	"	"	"
1916 Jan. 25	100	"	"	"
Apr. 7	50	"	"	"

The movement in the joint has been slow, but progressive. At one time, in August, 1915, extension became slightly limited. A plaster cast was applied for three weeks, and full extension returned. Whether or not this was a slight reawakening of the disease, I am not prepared to say. The outline shown was taken May 1, 1916.

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All of these cases have been under continuous hospital care, and every effort made to determine the exact influence of radium on the general, as well as the local, condition. The temperature, pulse and respiration, the blood pressure, the blood picture, the urinalysis, weight, the general condition as expressed by the patient, as well as observed by the examiner, have all been studied.

No general effect was noted other than that accompanying an excellent tonic. There were no deleterious constitutional effects whatsoever. Each patient expressed himself as feeling better under the radium treatment than he had before. I am quite aware that such a statement has little positive value, but negatively it is worthy of mention.

The results locally were more or less definite, even before any mobility was expressed. At first there was slight discomfort, but never any distinct pain. The patient expressed the feeling of looseness in the knee. This "looseness" or lessening of the stiffness was more noticeable in the mornings than it was after use. When movement began to be perceptible, it was noted that the knee assumed a slightly flexed position, and was straightened with slight difficulty. This did not seem to be the same expression of muscular spasm as is met with in acute kneejoint disease, but rather an uncertainty of the muscles as to whether or not they should relax as motion increased. It would sometimes be so difficult, after very much use, fully to extend the knee, that in several instances a mobilization with plaster of Paris, or a Thomas knee splint, was resumed for a week or ten days. As this loss of extension usually disappeared during the night, I do not think mobilization is necessary, but we felt safer in so doing. Slight stiffness was mentioned as being present in some of the cases, after sitting down with the knee flexed as fully as possible; however, this gave us no further concern. At no time was there any heat or swelling in any of these knees.

It may be that this treatment can be hastened with perfect safety by giving larger doses. Furthermore, it may be that after some mobility is obtained, and the patient is more or less saturated with radium, that forcible correction may be done, under an anesthetic, without the danger which is usually present.

These and other questions which arise regarding this use of radium, I hope to be able to answer when my research work is finished. I wish it to be distinctly understood that this is purely a preliminary report,

and offered at this meeting to encourage others to join in determining the place of radium in the armamentarium of the orthopedic surgeon.

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Edward M. Foote, M. D. (New York.) The Place of Radium in Surgery. Annals of Surgery, Vol. LXV., pp. 273-8, March, 1917. Radium's place in the treatment of tumors is still an uncertain one. Ten year's experience with it on the part of many experimenters, hundreds of articles in the medical press, even the monthly issue of several special journals, the publication of many books and endless discussions in medical society meetings have not resulted in fixing its value with any degree of definiteness.

At the present time there are some men who say that it has little or no value; while there are others who believe that it is destined to take the place of the knife in the treatment of tumors. Between these two extremes are scattered the opinions of the majority of surgeons, but these opinions have not yet grouped themselves around generally accepted truths.

In a review of this character it is unnecessary to refer to the technicalities of radium treatment; but one cannot too strongly urge upon all who write reports of cases, the great desirability of an exact description of patient and treatment. Wood states that there are only three factors of importance in the action of radium on tumor tissue: viz., time of exposure, dosage of radium and the distance between the radium and the tumor. In any report these data should invariably be given, as well as the nature of the tumor, its position and its bulk as nearly as this can be ascertained by surface measurements and by palpation.

When I first began a review of the reports on radium published in the last two years, I thought it might be possible to summarize them so as to draw fairly definite conclusions. The indefiniteness of statement in these reports, and especially in the reports from individuals, makes any such summary impossible; but there is reason to hope that within a comparatively short time, some generalizations may be possible in connection with the reports from radium institutions. For example, the radium institute of London has published its reports for 1912, 1913, and 1914. This institution is said to deal only with inoperable cases. Omitting the patients who were seen but not treated, the totals for these three years were 539, 654, and 594, of which the cures and apparent cures numbered the first year about 15 per cent., the second and third years about 11 per cent. of the totals. Possibly the war may have had some effect on the number of persons applying for treatment in 1914*. If not, and no other local cause existed to explain the very small increase in attendance, it seems a fair inference that the patients treated were not very favorably impressed with the results. A few more annual reports will bring this point out more clearly. It is absolutely certain that the future of any new method of treatment depends for more on what the patients think of it than it does on what the doctors think of it.

One of the generally accepted facts about radium is its ability to destroy tumor tissue. The way in which this is accomplished has given rise to much discussion, out of which has arisen the theory of the

* The report, for the years 1915-16, just issued, shows a total of 1400 patients for these two years.—Ed.

"selective action of radium." Some men have denied that it has a selective action upon the tumor cell; but most of those who have considered this question admit that it exists in some form. For practical purposes it makes little difference whether the radium attacks the tumor cells simply because they are less resistant than the normal cells of the body; or whether there is some really "selective action" in the stricter sense of the word. One writer has even suggested that the influence of radium upon cancer cells produces antibodies which may be useful in causing the disappearance of metastatic nodules, but this is pure speculation.

If then radium has a destructive effect upon tumor tissue "selective" to the extent of sometimes causing its disappearance while injuring the normal tissue only temporarily, the next important question to be settled is this, "What kind of tumors are susceptible to its influence?" Nearly every writer gives a different answer to this question, but there are a few points of agreement nevertheless. It is generally admitted that radium causes the disappearance of keloids, which may be called tumors by courtesy, of lymphangiomata and of basal-celled epitheliomata in very early stages or if they are superficial. All of these growths, it may be noticed in passing, are either on the surface or so near to it that only a thin layer of skin intervenes between the radium and the normal cells. Beyond this general statement, there are instances reported by different writers of the disappearance after exposure to radium of almost every kind of tumor in almost every part of the body; but thus far no rule has been discovered by which the effect of radium in any particular case can be predicted with certainty.

There is, however, one group of tumors in which success has frequently been noticed, and another in which failure from treatment has been very generally admitted. In the first group should be placed the sarcomata and in the second group the prickle-celled epitheliomata. The rapidity with which one sarcoma will destroy the human body while another is driven out by some apparently inadequate cause (for example Coley's fluid), forms a riddle which medical science has not yet solved. It is not to be wondered at that the behavior of these tumors to radium is therefore variable. Even a melanotic sarcoma of multiple form has been said to disappear after the use of radium as if by magic.

In another group of tumors radium has frequently been employed and as some have claimed, with great success; although these claims have been disputed by others. These are tumors of the cervix and body of the uterus and tumors of the ovaries. The admitted facts in this connection are the production of amenorrhoea, the drying up of foul vaginal discharge and the cicatrization of ulcers. The skeptics claim that this is the sum total of the effect of radium in these cases. There is no doubt of the artificial sterility produced in these patients by the use of large doses of radium repeatedly applied for several hours at a time. It is also produced in the nurses who have to wait on the patients during the attacks of nausea caused by the radium treatment.

This amenorrhoea is sufficient to check the hemorrhage from uterine fibroids and probably sufficient to explain the partial shrinkage in the tumors which sometimes occurs. Similar changes sometimes take place at the normal menopause. But it seems a little far-fetched to explain the disappearance of cancer of the cervix, much less of the body of the uterus, as due to this artificial sterility, for no such phenomenon takes

place at the normal menopause; yet there are not wanting men who claim to have affected repeatedly the cure of cancer which extended well into the pelvis. Perhaps the present attitude of conservative men who regard radium favorably is fairly stated by Ransohoff, who advises operation in operative uterine cases, but uses radium to stop the discharge and hemorrhage and destroy the cauliflower masses, when these symptoms develop in inoperable cases. The improvement of symptoms which results is in most cases only temporary.

It seems very unlikely that a patient having secondary cancerous nodules in lymph-glands or elsewhere can be cured by radium. We have been repeatedly told that its influence after penetrating an inch of tissue is practically *nil.* A palpable metastatic nodule will often be near the surface, but by the time it is recognizable for radium treatment there are almost sure to be other metastatic nodules in other places, some of them quite inaccessible for recognition or treatment.

How explain then the reported instances of disappearance of cancer when lymphatic glands were involved?

There are three possible explanations: First, lymph-glands are often enlarged from other causes. Almost everybody has palapable lymph-glands in some situation. Second, ulcerative cancers often produce enlargement of the regional glands, when if these glands are examined microscopically it will sometimes be found that they are enlarged as a result of inflammation and are not cancerous at all. Third, in some cases even non-ulcerating cancers may be sufficiently irritating to produce glandular enlargement.

This brings us to the last question and perhaps the most important of all. Shall a patient having cancer in operable condition be advised to have an operation or treatment by radium?

A fair answer to this question based on the published articles seems to be that operation should have the preference in cancer so situated that operation gives a fair chance of cure. In the present state of our knowledge, I think a man does his patient a grave injustice if he advises radium for a primary prickle-celled epithelioma, or for any primary cancer of considerable bulk, if the conditions are favorable for its removal.

Primary basal-celled epitheliomata of the face, lymphangiomata, and fibroids of the uterus, angiomata and keloids may all be safely treated with radium. In the case of large rapidly growing tumors, sarcomatous or otherwise, so situated that operation is likely to prove unsuccessful or to have a high mortality, radium may be tried; but the proper place to test it is still in the recurrences. Many of them are situated near the surface, so that radium has the best opportunity for its action, and the investigator can determine the effect of treatment by inspection, palpation and measurement, and can remove tissue for microscopic examination from time to time. This is the proper field for research and it can be carried out without taking away some patient's best chance of a cure by surgical removal of his tumor.

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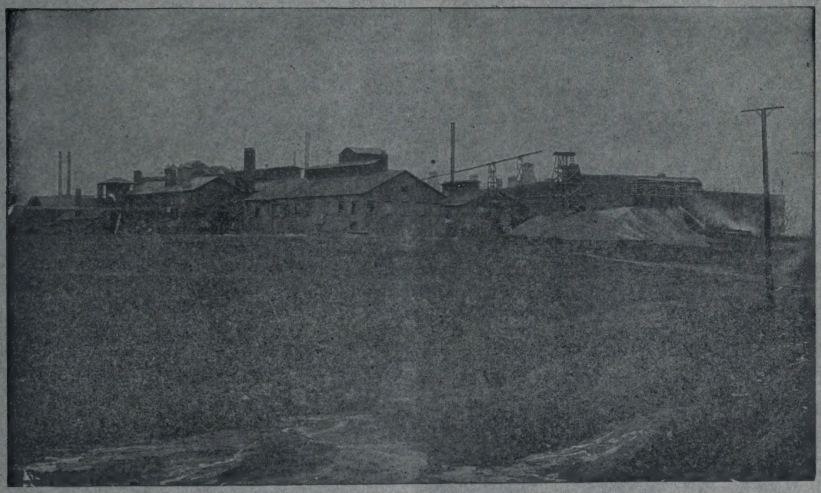

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